

REMARKS

Claims 1, 27-28, 42, 48, 51 and 54-58 are pending in this application. Claims 1, 27-28, 42, 48, 51 and 54-58 were variously rejected under 35 U.S.C. § 112, first paragraph. Claims 1, 27-28, 42, 48, 51 and 54-58 were rejected under 35 U.S.C. § 112, second paragraph. Claims 54-58 were rejected under 35 U.S.C. § 103. Claims 56 and 58 were objected to.

By this amendment, claims 1, 56 and 58 have been amended and new claim 61 has been added without prejudice or disclaimer of any previously claimed subject matter. Support for the amendments can be found, *inter alia*, throughout the specification. Support for the amendment to claim 1 is found, *inter alia*, at page 8, lines 13-18 and in original claim 5. New claim 61 is derived from previous claim 1 and support for new claim 61 is found, *inter alia*, in original claim 4.

The amendments are made solely to promote prosecution without prejudice or disclaimer of any previously claimed subject matter. With respect to all amendments and cancelled claims, Applicants have not dedicated or abandoned any unclaimed subject matter and moreover have not acquiesced to any rejections and/or objections made by the Patent Office. Applicants expressly reserve the right to pursue prosecution of any presently excluded subject matter or claim embodiments in one or more future continuation and/or divisional application(s).

Applicants have carefully considered the points raised in the Office Action and believe that the Examiner's concerns have been addressed as described herein, thereby placing this case into condition for allowance.

Claim Objections

Applicants maintain that claims 56 and 58 were not redundant as asserted by the Examiner. However, claims 56 and 58 have herein been amended in the interest of expediting prosecution of this application. Applicants respectfully request reconsideration and withdrawal of the objections.

Rejections under 35 U.S.C. §112, first paragraph*Written Description*

Claims 1, 27-28, 42, 48, 51 and 54-58 were rejected under 35 U.S.C. §112, first paragraph, as allegedly containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. Applicants respectfully traverse this ground for rejection.

Applicants maintain that nucleic acid sequences encoding microbial endo-glucanases were well known in the art at the time the application was filed and, accordingly, Applicants are not required to present the sequences in the specification. The specification provides examples of endo-glucanases for use in the claimed invention along with Enzyme Classification numbers, such as endo-1, 3- β -glucanase (E.C. 3.2.1.6), endo-1, 4- β -glucanase (E.C. 3.2.1.4) and α -amylase (E.C. 3.2.1.1), for example, at page 6, lines 22-23 and 31-32. With such information, the skilled artisan could readily identify microbial endo-glucanase encoding nucleic acid sequences in literature and sequence databases.

At the Examiner's request, submitted herewith are 12 exemplary references providing endo-glucanase encoding nucleic acid sequence information from a wide variety of microbial species, including seven of the references listed in Exhibit B included with the response to the January 10, 2003 Office Action, filed May 12, 2003. Applicants respectfully point out that these references include not only endo-glucanase sequences isolated from a variety of bacteria¹ but also such sequences isolated from a variety of fungi² and from the cellular slime mold *Dictyostelium*.

¹ For example, a variety of *Bacillus subtilis* strains, alkalophilic *Bacillus* species, *Cellulomonas* species, *Clostridium* species, *Erwinia* species and *Pseudomonas* species.

² For example, *Robillarda* species, *Schizophyllum* species and *Trichoderma* species.

Thus, Applicants respectfully submit that nucleic acid sequences encoding many microbial endoglucanases were known in the art at the time the application was filed.

The written description requirement “may be satisfied if in the knowledge of the art the disclosed function is sufficiently correlated to a particular, known structure” and compliance with the requirement “is essentially a fact-based inquiry that will ‘necessarily vary depending on the nature of the invention claimed.’” See *Amgen, Inc. v. Hoechst Marion Roussel, Inc. and Transkaryotic Therapies, Inc.*, USPQ 65 USPQ2d 1385 (Fed. Cir. 2003); *Enzo Biochem, Inc. v Gen-Probe, Inc.*, 63 USPQ2d 1609 (Fed. Cir. 2002). Applicants respectfully submit that the specification in combination with that known in the art adequately describes possession of the claimed genus to one skilled in the art.

In view of the foregoing, Applicants respectfully submit that a *prima facie* case of lack of written description has not been established and that the written description requirement has been met.

Enablement

Claims 1, 27-28, 42, 48, 51 and 54-58 were rejected under 35 U.S.C. §112, first paragraph, for allegedly not enabling any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with the claims. Applicants respectfully traverse this rejection.

The invention is directed to a method of modifying the polysaccharide/saccharide composition of a plant or plant organ by growing a transgenic plant containing a nucleotide sequence encoding a glucanase, an enzyme that degrades polysaccharides into saccharides. The nucleotide sequence encoding the glucanase is operably linked to a regulatory sequence which

directs expression of the enzyme. The invention is also directed to a recombinant DNA expression cassette for use in the method and to transgenic plants generated by the method or with the expression cassette. In the amended claims, a microbial endo-glucanase is expressed and the expressed glucanase modifies the polysaccharide/saccharide composition of the plant such that the saccharide composition is increased relative to a nontransgenic plant.

The Examiner admits that “plants and methods for plant transformation were well known in the art” but states that “methods for making directed alterations to plant phenotype were highly unpredictable.” Office Action, pages 4-5. Applicants respectfully submit that making alterations to plant phenotype as claimed was not “highly unpredictable” and that the claimed invention is enabled by the specification.

As described above, exemplary endo-glucanases are presented in the specification and nucleic acid sequences encoding microbial endo-glucanases were known in the art at the time of filing. The activity of endo-glucanases and techniques to assess endo-glucanase activity are well known in the art. Appropriate transcriptional regulatory sequences are set forth starting on line 24 of page 9 and useful targeting leader sequences are set forth starting at line 25 on page 10. Suitable plants are illustrated on page 8 starting at line 25. The examples demonstrate expression of a glucanase at various sites, e.g. leaves, roots and fruit, of transgenic plants results in an increase in saccharide composition as compared with a nontransgenic plant.

The specification, including the examples, illustrates the operation of the invention. Following these teachings using conventional materials is not seen to involve undue experimentation. The stated object is to modify polysaccharide/saccharide composition such that there is an increase in the saccharide composition of the plant or plant organ. The nature of the modification, e.g. an increase in the presence of oligo- and/or monosaccharides, is described as well

as its monitoring using conventional assays. Such alteration to a plant phenotype is not highly unpredictable and would not create undue experimentation to obtain or detect.

Thus, Applicants submit that the specification adequately teaches the skilled artisan how to make and use, i.e., enables, the claimed invention.

The Examiner points to the previously cited Harpster³ and Carvalho⁴ references as evidence of unpredictability of gene expression in transgenic plants. Harpster describes over expression of a pepper endo-glucanase in a transgenic tomato and observes a 24-37% reduction in non-xyloglucan glycans, a loss of other higher molecular weight matrix glycans but no obvious differences in plant morphology.⁵ Thus, Harpster demonstrates that expression of a polysaccharide degrading enzyme (endo-glucanase) in a transgenic plant does indeed result in a modification of the polysaccharide/saccharide composition of the plant. The teachings of Harpster do not support any doubt of the teachings of the specification or provide evidence for the alleged unpredictability of the claimed invention.

Carvalho also describes the use of plant-derived genes for transformation to plants, in this case within the same genus. Carvalho observes a transgene “gene silencing” phenomenon in only one of five transgenic plant lines, and only in plants homozygous for the transgene derived from that one particular line. Thus, the great majority of the transgenic plant lines reported in Carvalho express the transgene apparently as expected and do not provide evidence for the alleged unpredictability of the claimed invention or for any doubt of the teachings of the specification. Applicants respectfully remind the Examiner that absolute predictability is not required to satisfy 35 U.S.C. §112, first paragraph.

³ Harpster et al. (2002, *Plant Molecular Biology* 50:357-369; “Harpster”)

⁴ Carvalho et al. (1992, *EMBO J.* 11:2595-2602; “Carvalho”)

⁵ See Harpster, for example, pages 364-366 and Figures 5A and 6.

Applicants respectfully submit that these references when taken in their entirety do not support the alleged state of unpredictability with regard to the claimed invention and thus, do not provide acceptable documentation or sound scientific reasoning to support any doubt of the teachings of the specification. See, for example, *In re Marzocchi*, 439 F2d 220, 224, 169 USPQ 367, 370 (CCPA 1971). Unless such documentation and/or scientific reasoning are adduced, the statements made in the specification are to be taken at face value.

Thus, Applicants respectfully submit that a *prima facie* case for lack of enablement has not been established and that the claimed invention is enabled by the specification. Accordingly, the pending claims are in compliance with the enablement requirements.

In sum, Applicants submit that the pending claims fall within the subject matter that is enabled and described by the specification. Accordingly, Applicants respectfully request reconsideration and withdrawal of the rejections under 35 U.S.C. § 112, first paragraph.

Rejection under 35 U.S.C. §112, second paragraph

Claims 1, 27-28, 42, 48, 51 and 54-58 were rejected under 35 U.S.C. §112, second paragraph, as allegedly being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Applicants respectfully traverse this rejection.

Although Applicants continue to believe that the claims were sufficiently definite when considered in view of the specification and the understanding of those of skill in the art, Applicants have attempted to respond to the concerns of the Examiner in order to enhance clarity and to facilitate disposition of the present case.

The invention is directed to modifying the polysaccharide/saccharide composition of a plant or plant organ through expression of a microbial glucanase, a polysaccharide degrading enzyme, in the plant. As shown in the Examples, expression of a microbial glucanase in a transgenic plant results in an accumulation of saccharides in the plant. Thus, the polysaccharide/saccharide content of the plant or plant organ is altered. In the amended claims, the microbial glucanase is an endo-glucanase and the polysaccharide/saccharide composition is modified such that there is an increase in the saccharide composition of the plant expressing the transgene.

Applicants have also amended the claims to clarify that the leader sequence is to target the expressed enzyme to an organelle or cellular location, such as to a chloroplast. Such targeting leaders sequences are known in the art and described in the specification, for example at page 10, line 25, to page 11, line 2.

In view of the foregoing, Applicants respectfully request reconsideration and withdrawal of the rejection under 35 U.S.C. § 112, second paragraph.

Rejection under 35 U.S.C. §103

Claims 54-58 and were rejected under 35 U.S.C. §103(a) as allegedly unpatentable over Cornelissen *et al.* (U.S. Patent 6,066,491, effective filing date January 29, 1991) or Cornelissen *et al.* (EP 440304, published August 7, 1991) either in view of Baird *et al.* (*J. Bacteriol.* 172:1576-1586, 1990). Applicants respectfully traverse this rejection.

As pointed out in the response to the January 10, 2003 Office Action, filed May 12, 2003, the instant application claims priority to a European Patent application filed prior to the U.S. effective filing date of the cited Cornelissen *et al.* U.S. patent and prior to the publication date of the

cited Cornelissen *et al.* European Patent application. Thus, the Cornelissen *et al.* references are not available as prior art under any 35 U.S.C. §102 section and accordingly, not available for citation under 35 U.S.C. §103.

The instant application claims priority under 35 U.S.C. §119 to the application EPO 90202434.8 filed September 13, 1990. Applicants' representative note that this application number was incorrectly stated in the response filed May 12, 2003 and apologizes for any confusion the incorrect number may have caused. This application number is the same as the priority application number recited in declaration for the instant application.⁶ As noted on the declaration, International application No. PCT/NL91/00171 was filed September 13, 1991 claiming priority to the EPO application and designating the U.S. U.S. application number 07/849,422 was filed under 35 U.S.C. §371 on June 12, 1992.

Submitted herewith (attached as Appendix A) is a copy of EPO 90202434.8 as requested by the Examiner. Applicants respectfully point out that the instant invention is adequately described in this priority document. Thus, the Cornelissen *et al.* references are not available as prior art under 35 U.S.C. §103.

Baird describes cloning and sequence analysis of a *Bacillus polymyxa* endo-glucanase gene and demonstrated sequence similarity between it and endo-glucanase genes from *Bacillus circulans* and from *Clostridium thermocellum*. Baird neither describes nor suggests the generation of DNA expression cassettes for expression of the microbial endo-glucanase in transgenic plants. Baird does not describe or suggest a transgenic plant containing a nucleotide sequence encoding a microbial endo-glucanase. Further, Baird provides no motivation for one skilled in the art to modify the teachings therein to arrive at the presently claimed invention.

⁶ The original declaration/oath was filed June 12, 1992 for Application Serial No. 07/849,422.

Accordingly, Baird does not support *prima facie* obviousness with regard to the claimed invention. Applicants respectfully submit that a *prima facie* case of obviousness has not been established. Applicants respectfully request reconsideration and withdrawal of the rejections under 35 U.S.C. §103.

CONCLUSION

Applicants believe that all issues raised in the Office Action have been properly addressed in this response. Accordingly, reconsideration and allowance of the pending claims is respectfully requested. If the Examiner feels that a telephone interview would serve to facilitate resolution of any outstanding issues, the Examiner is encouraged to contact Applicants' representative at the telephone number below.

In the unlikely event that the transmittal letter is separated from this document and the Patent Office determines that an extension and/or other relief is required, Applicants petition for any required relief including extensions of time and authorize the Assistant Commissioner to charge the cost of such petitions and/or other fees due in connection with the filing of this document to Deposit Account No. 03-1952 referencing docket no. 261922003302.

Dated: April 8, 2004

Respectfully submitted,

By Karen R Zachow
Karen R. Zachow
Registration No.: 46,332
MORRISON & FOERSTER LLP
3811 Valley Centre Drive, Suite 500
San Diego, California 92130
(858) 720-5191